

C⁵ allow the agent to modulate the activity of the polypeptide.

REMARKS

Status of the Claims

Claims 1-37 are pending. Claims 1, 3-8, 15-17, 21, 31, and 32 have been withdrawn. Claims 2, 9, 18 and 19 have been amended. Support for the amended claims can be found in the original claims as well as the specification. Accordingly, no new matter has been added by way of amendment. Reexamination and reconsideration of the claims as amended are requested.

REJECTIONS:

I. Rejection of claims under the doctrine of obviousness-type double patenting.

Claims 2, 9-14, 18-20, 22-30, and 33-37 were rejected under the provisionally created doctrine of obviousness-type double patenting over claims 73, 74, 81, and 88-96 in copending provisional application no. 09/464,685. Upon issuance of a Notice of Allowance in the instant application, Applicants will file a Terminal Disclaimer in compliance with 37 C.F.R. 1.321(c) to overcome this double patenting rejection. Therefore, Applicants respectfully traverse this rejection.

II. The Rejection of Claims Under 35 U.S.C. § 101 Should Be Withdrawn.

Claims 2, 9-14, 18-20, 22-30, and 33-37 were rejected under §101 for failing to meet utility requirements. The Examiner has rejected claims 2, 9-14, 18-20, 22-30 and 33-37 for lack of a patentable utility under § 101. It is stated in the Office Action that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. However,

Applicants respectfully disagree with this statement for the reasons detailed below.

First, the Applicant's disclosure establishes a well-established utility for the claimed subject matter satisfying the requirements of 35 U.S.C. §101. Applicant has demonstrated that the polypeptide of the invention is a G protein-coupled receptor. It is known to those of skill in the art that G protein-coupled receptors have a well-established utility as targets for the diagnosis and treatment of G protein-coupled receptor-related diseases. Page 2, lines 3-5 of the specification states that G protein-coupled receptor genes and gene products are potential causative agents in disease, and the art is replete with examples of G-protein coupled receptors that serve as known or potential targets in the diagnosis and treatment of disease (reviewed, for example, in Spiegel (1993) *J. Clin. Invest.* 92:1119-1125; McKusick (1993) *J. Med. Genet.* 30:1-26; Mills and Duggan (1994) *Trends Biotechnol* 12:47-49; and Stadel *et al.* (1997) *TIPS* 18:430-437). In fact, Stadel *et al.* (ibid.) state that, "Historically, the superfamily of GPCR's has proven to be among the most successful drug targets and consequently these newly isolated orphan receptors have great potential for pioneer drug discovery."

The utility of members of the G-protein coupled receptor family as known or potential drug targets results not only from their important cellular functions and their association with human diseases, but also from the fact that their biological function dictates that their activity is modulated by association with small-molecule ligands. It is well known in the art that polypeptides whose biological activities are controlled by small molecules are extremely useful in the development of therapeutics, as they readily lend themselves to the process of rational drug design. Thus, the receptor of the invention belongs to a family of proteins for which there is a well-established utility. This conclusion alone satisfies the requirements of 35 U.S.C. § 101 and warrants the withdrawal of the rejection.

In concluding that applicants have not disclosed a substantial utility for the claimed invention, the Office Action misapplies the new Revised Interim Utility Guidelines Training Material Examples. The arguments presented in the Office Action indicating that the claimed invention lacks a substantial utility appear contrary to the examples cited in the Revised Interim Utility Guidelines Training Materials. Specifically, Example 10 in the Training Materials

appears analogous to the instant application.

Example 10 of the Revised Interim Utility Guidelines, which is directed to a sequence with a high degree of sequence similarity with a DNA ligase, appears analogous to the situation found in the instant application. Like Example 10, the claimed invention has been shown to share a high degree of sequence similarity with a protein of known function. Like Example 10, the protein of known function has a well-established utility. The well-established utility is the use as a target or reagent in the diagnosis and treatment of G-protein coupled receptor-mediated disorders (see above). Accordingly, based on analogy to Example 10, the present invention also meets the criteria for well-established utility. Specifically, the claimed invention is drawn to an antibody specific for SEQ ID NO:1, a method of screening agents which modulate the activity or expression of SEQ ID NO:1 and variants and fragments thereof. Accordingly the claimed invention meets the criteria for well-established utility.

In addition, the encoded polypeptide of Example 10 is accorded to have a specific and substantial utility according to the guidelines, despite the fact that the sequence has not been directly demonstrated to have DNA ligase activity, and that the substrate (i.e. single-stranded DNA or double-stranded DNA; blunt-ended DNA, 5' recessed ended DNA, 3' recessed ended DNA), co-factor requirements, and reaction conditions required to practice the invention are not disclosed. Thus, the very fact that the sequence of Example 10 has high sequence similarity with a known protein possessing well-established utility is sufficient to confer a specific, substantial, and credible utility upon the claimed sequence. As the claimed invention of the present application is analogous to the situation described in Example 10, the criteria for utility have been met.

Furthermore, the law is clear that the standard for assessing utility under 35 U.S.C. §101 is confined to assessing whether or not the requisite utility is asserted or well-established. In contrast to the Examiner's assertion, there is no requirement under §101 that the Applicant provide guidance as to how to use the claimed invention. Indeed, as noted above, in Example 10 there is no teaching of how to use the DNA ligase. The present application provides sequence similarity to a known protein and expression data of gene 2871 in various tissues (Figure 5).

Also, correlation with a wide spectrum of clinical disorders linked to GPCR expression is indicated in the art. In fact, the disclosed GPCR's belong to a family of polypeptides that are known targets for particular diseases. The utility of the instant invention is therefore substantial as G protein-coupled receptors have been demonstrated to have a "real-world" use in the development of drugs to treat a large number of disorders.

The Applicants contend that the specification discloses an invention that has a credible, specific and substantial utility. The specification discloses isolated, novel polypeptides encoded by novel DNA sequences that have homology to known GPCR proteins with uniquely characteristic and conserved domains. The specification teaches that the 2871 polypeptide has domains which are uniquely characteristic of GPCR proteins. These include three main structural domains, including the extracellular domain identified at residues 1 to about 42 in SEQ ID NO:1, the transmembrane domain at about residues 43 to 418 in SEQ ID NO:1, and the intracellular domain at about residues 319 to 359 in SEQ ID NO:1. Additionally, a uniquely characteristic GPCR signal transduction signature, DRY, is identified at residues 138-140 in the transmembrane domain.

Moreover, it is clearly the case that there are proteins which may not share high overall sequence homology yet they share high homology for certain domains and it is the domains which confer on each protein certain functional attributes which are related to the domain sequences. In fact it is well accepted that new proteins can evolve through the combination of different polypeptide domains (Rossmann *et al.* (1981) *Annu. Rev. Biochem.* 50:497-532). Accordingly, based on the applicant's disclosure, there is strong support for the assertion that SEQ ID NO:2 encodes a GPCR. Further, GPCR proteins have a well-established utility wherein they are involved in the transmission of signals to the interior of the cell. They respond to a diverse variety of agents including lipid analogues, amino acid derivatives, and small peptides. They are found in a wide variety of organisms. (*The G-Protein Linked Receptor/Facts Book* (1994) Watson *et al.* eds., Academic Press).

The polypeptides of the instant invention have been classified as GPCR molecules based on homology with known proteins and on shared protein domains. As noted above, it is well

recognized in the art that protein domains are predictive as to the activity of the protein. The instant invention is specifically drawn to antibodies which bind SEQ ID NO:1, methods of screening agents which modulate the activity or expression of SEQ ID NO:1 and variants and fragments of SEQ ID NO:1. Accordingly, there is a substantial utility already associated with the claimed invention. The criteria of a specific, substantial and credible utility of the claimed invention would be readily apparent to one of ordinary skill in the art, and consequently, the rejection under 35 U.S.C. § 101 should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn.

Claims 2, 9-14, 18-20, 22-30, and 33-37 were rejected under 35 U.S.C. § 112, first paragraph, as not being supported by either a well-established or a specific and substantial utility. As argued above, Applicant submits that the invention does have established utility and one of ordinary skill in the art would know how to use the claimed invention. The specification teaches numerous examples for how the novel 2871 polynucleotides and polypeptides can be used. These include: producing antibodies, in GPCR assays, in drug screening assays, in assays for identifying compounds that modulate receptor activity, for screening compounds for the ability to modulate or inhibit interaction between the receptor and the target protein, and for detecting the formation of a complex between the target and the GPCR.

As indicated above, the specification teaches that the novel 2871 polypeptides contain the unique domains characteristic of GPCR proteins and thus would inherently contain the structural elements and functional properties well established for GPCR proteins which can be involved in a multitude of cellular processes and cellular signaling events as disclosed in the specification. It is not necessary for the patent document to read like a production specification. A requirement for some experimentation does not prevent the satisfaction of the enablement requirement (*Northern Telecom, Inc. v. Datapoint Corp.*, 15 U.S.P.Q.2d1321, 1329 (Fed. Cir. 1990)). As established above, the present invention possesses a specific, substantial, and credible utility, and accordingly, it cannot be asserted that a person of ordinary skill in the art

would not know how to use the claimed invention.

Furthermore, the law has never required an applicant to know the specific method or mechanism by which his invention operates. For example, the Court of Appeals for the Federal Circuit has long held that, "it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests, nor is the inventor's theory or belief as to how his invention works a necessary element in the specification to satisfy the enablement requirement of 35 U.S.C. § 112." *Cross v. Iizuka*, 753 F.2d 1040, 1042 (footnote 3), 224 USPQ 739 (Fed. Cir. 1985). In a more recent case, the Federal Circuit again stated, "[i]t is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." *In re Cortright*, 163 F.3d 1353, 1359 (Fed. Cir. 1999) (citations omitted) (the court reversed the Board's rejection of certain claims to a treatment for baldness). The court also noted that, "[t]he PTO cannot make this type of rejection [lack of utility], however, unless it has reason to doubt the objective truth of the statements contained in the written description" (id. at 1357). The PTO must provide evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility before the burden shifts to applicant to provide rebuttal evidence.

The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn.

Claims 2, 9-14, and 18-20 were rejected under 35 U.S.C. § 112, second paragraph, for failing to point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2, 9-14 and 18-20 were considered indefinite since they depended on non-elected claim 1.

Claims 2, 9, 18 and 19 have been amended. These newly amended claims are drafted as independent claims and are not dependent on a non-elected claim. These claims are also drafted to provide proper antecedent support for any dependent claims. Therefore, applicants respectfully request that this rejection be withdrawn.

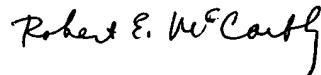
CONCLUSIONS

Applicants believe that the present application is now in a condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. The Applicants note that upon an indication of allowability, the Applicants may choose to rewrite claims with Markush groups into separate and independent claims.

Prompt and favorable consideration of the foregoing amendments, and entry of the same into the present application, are respectfully requested.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



Robert E. McCarthy
Patent Agent
Registration No. 46,044

ALSTON & BIRD LLP
Post Office Drawer 34009
Charlotte, NC 28234
Tel Raleigh Office (919) 420-2200
Fax Raleigh Office (919) 420-2260

